CLAIMS

What is claimed is:

1.   A method of detecting a predisposition to cancer in an animal, said method comprising:

(i) providing a biological sample from said animal;

(ii) detecting the level of *CYP24* within said biological sample; and

(iii) comparing said level of *CYP24* with a level of *CYP24* in a control sample taken from a normal, cancer-free tissue; wherein an increased level of *CYP24* in said biological sample compared to the level of *CYP24* in said control sample indicates a predisposition to cancer in said animal.

2.   The method of claim 1, wherein said level of *CYP24* is detected by determining the copy number of *CYP24* genes in the cells of said biological sample.

3.   The method of claim 2, wherein said copy number is measured using Comparative Genomic Hybridization (CGH).

4.   The method of claim 1, wherein said copy number is determined by hybridization to an array of nucleic acid probes.

5.   The method of claim 3, wherein said Comparative Genomic Hybridization is performed on an array.

6   The method of claim 1, wherein said level of *CYP24* is detected by measuring the level of *CYP24* mRNA in said biological sample, wherein an increased level of *CYP24* RNA in said sample compared to *CYP24* RNA in said control sample indicates a predisposition to cancer.

7.   The method of claim 6, wherein said level of *CYP24* mRNA is measured in said biological sample and said control sample at the same vitamin D receptor activity or the *CYP24* mRNA levels are normalized to the level of vitamin D receptor activity in the sample and control.

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1   8.   The method of claim 6, wherein said level of *CYP24* mRNA is
2   measured by hybridization to one or more probes on an array.

1   9.   The method of claim 1, wherein said level of *CYP24* is detected by
2   measuring the level of *CYP24* protein in said biological sample, wherein an increased level
3   of *CYP24* protein in said sample as compared to *CYP24* protein in said control sample
4   indicates a predisposition to cancer.

1   10.   The method of claim 9, wherein the level of *CYP24* protein is
2   measured in the biological sample and the control sample at the same vitamin D receptor
3   activity or the protein levels are normalized to the level of vitamin D receptor activity in the
4   sample and control.

1   11.   The method of claim 1, wherein said level of *CYP24* is detected by
2   measuring the level of 25-hydroxyvitamin D3 24-hydroxylase enzyme activity in said
3   biological sample, wherein an increased level of 25-hydroxyvitamin D3 24-hydroxylase
4   enzyme activity in said sample as compared to 25-hydroxyvitamin D3 24-hydroxylase
5   enzyme activity in said control sample indicates a predisposition to cancer.

1   12.   The method of claim 11, wherein said level of 25-hydroxyvitamin D3
2   24-hydroxylase activity is measured in said biological sample and said control sample at the
3   same vitamin D receptor activity or the activity levels are normalized to the level of vitamin
4   D receptor activity in the sample and control.

1   13.   The method of claim 1, wherein said animal is a mammal selected
2   from the group consisting of humans, non-human primates, canines, felines, murines,
3   bovines, equines, porcines, and lagomorphs.

1   14.   The method of claim 1, wherein said biological sample is selected
2   from the group consisting of excised tissue, whole blood, serum, plasma, buccal scrape,
3   saliva, cerebrospinal fluid, and urine.

1   15.   The method of claim 1, wherein the difference between said increased
2   level of *CYP24* in said biological sample and the level of *CYP24* in said control sample is a
3   statistically significant difference.

1   16.   The method of claim 1, wherein said increased level of *CYP24* in said
2 biological sample is at least about 2-fold greater than the level of *CYP24* in said control
3 sample.

1   17.   The method of claim 1, wherein said increased level of *CYP24* in said
2 biological sample is at least about 4-fold greater than said level of *CYP24* in said control
3 sample.

1   18.   A method of estimating the survival expectancy of an animal with
2 cancer, said method comprising:
3   (i) providing a biological sample from said animal;
4   (ii) detecting the level of *CYP24* within said biological sample; and
5   (iii).comparing said level of *CYP24* with the level of *CYP24* in a
6 control sample taken from a normal, cancer-free tissue;
7 wherein an increased level of *CYP24* in said biological sample compared to the level of
8 *CYP24* in said control sample indicates a reduced survival expectancy in said animal
9 compared to in an animal with cancer that has a normal level of *CYP24*.

1   19.   The method of claim 18, wherein said level of *CYP24* is detected by
2 determining the copy number of *CYP24* genes in the cells of said animal.

1   20.   The method of claim 19, wherein said copy number is determined by
2 hybridization to an array of nucleic acid probes.

1   21.   The method of claim 19, wherein said copy number is measured using
2 Comparative Genomic Hybridization.

1   22.   The method of claim 21, wherein said Comparative Genomic
2 Hybridization is performed on an array.

1   23.   The method of claim 18, wherein said level of *CYP24* is detected by
2 measuring the level of *CYP24* mRNA in said biological sample, wherein an increased level
3 of *CYP24* RNA in said sample as compared to *CYP24* RNA in said control sample indicates
4 a reduced survival expectancy.

1   24.   The method of claim 23, wherein said level of *CYP24* mRNA is

2   measured in said biological sample and said control sample at the same vitamin D receptor

3   activity or the activity levels are normalized to the level of vitamin D receptor activity in the

4   sample and control.

1   25.   The method of claim 18, wherein said level of *CYP24* is detected by

2   measuring the level of *CYP24* protein in said biological sample, wherein an increased level

3   of *CYP24* protein in said sample as compared to *CYP24* protein in said control sample, at a

4   given level of vitamin D receptor activity indicates a reduced survival expectancy.

1   26.   The method of claim 18, wherein said level of *CYP24* is detected by

2   measuring the level of 25-hydroxyvitamin D3 24-hydroxylase enzyme activity in said

3   biological sample, wherein an increased level of 25-hydroxyvitamin D3 24-hydroxylase

4   enzyme activity in said sample as compared to 25-hydroxyvitamin D3 24-hydroxylase

5   enzyme activity in said control sample indicates a reduced survival expectancy.

1   27.   The method of claim 26, wherein said level of 25-hydroxyvitamin D3

2   24-hydroxylase activity is measured in said biological sample and said control sample at the

3   same vitamin D receptor activity or the activity levels are normalized to the level of vitamin

4   D receptor activity in the sample and control.

1   28.   The method of claim 18, wherein said animal is a mammal selected

2   from the group consisting of humans, non-human primates, canines, felines, murines,

3   bovines, equines, porcines, and lagomorphs.

1   29.   The method of claim 18, wherein said biological sample is selected

2   from the group consisting of excised tissue, whole blood, serum, plasma, buccal scrape,

3   saliva, cerebrospinal fluid, and urine.

1   30.   The method of claim 18, wherein the difference between said

2   increased level of *CYP24* in said biological sample and the level of *CYP24* in said control

3   sample is a statistically significant difference.

1   31.   The method of claim 18, wherein said increased level of *CYP24* in
2 said biological sample is at least about 2-fold greater than the level of *CYP24* in said control
3 sample.

1   32.   The method of claim 18, wherein said increased level of *CYP24* in
2 said biological sample is at least about 4-fold greater than the level of *CYP24* in said control
3 sample.

1   33.   A method of treating cancer in an animal, said method comprising:
2   (i) providing a biological sample from said animal;
3   (ii) detecting the level of *CYP24* within said biological sample;
4   (iii) comparing said level of *CYP24* with a level of *CYP24* in a control
5 sample from a normal, cancer-free tissue; and
6   (iv) selecting and performing a cancer therapy in those animals having
7 an increased level of *CYP24* compared to the level of *CYP24* in said control sample.

1   34.   The method of claim 33, wherein said cancer therapy is selected from
2 the group consisting of chemotherapy, radiation therapy, surgery, antihormone therapy, and
3 immunotherapy.

1   35.   The method of claim 34, wherein said cancer therapy is an adjuvant
2 cancer therapy.

1   36.   The method of claim 33, wherein said level of *CYP24* is detected by
2 determining the copy number of *CYP24* genes in the cells of said animal.

1   37.   The method of claim 36, wherein said copy number of *CYP24* genes is
2 determined by hybridization to an array of nucleic acid probes.

1   38.   The method of claim 36, wherein said copy number of *CYP24* genes is
2 measured using Comparative Genomic Hybridization (CGH).

1   39.   The method of claim 26, wherein said Comparative Genomic
2 Hybridization is performed on an array.

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40. The method of claim 33, wherein said level of *CYP24* is detected by measuring the levels of *CYP24* mRNA in said biological sample, wherein an increased level of *CYP24* RNA in said sample as compared to *CYP24* RNA in said control sample indicates the need for an adjuvant cancer therapy.

41. The method of claim 40, wherein said level of *CYP24* RNA is measured in said biological sample and said control sample at the same vitamin D receptor activity or the activity levels are normalized to the level of vitamin D receptor activity in the sample and control.

42. The method of claim 33, wherein said level of *CYP24* is detected by measuring the level of *CYP24* protein in said biological sample, wherein an increased level of *CYP24* protein in said sample as compared to *CYP24* protein in said control sample indicates the need for an adjuvant cancer therapy.

43. The method of claim 42, wherein said level of *CYP24* protein activity is measured in said biological sample and said control sample at the same vitamin D receptor activity or the activity levels are normalized to the level of vitamin D receptor activity in the sample and control.

44. The method of claim 33, wherein said *CYP24* level is detected by measuring the level of 25-hydroxyvitamin D3 24-hydroxylase enzyme activity in said biological sample wherein an increased level of 25-hydroxyvitamin D3 24-hydroxylase enzyme activity in said sample as compared to 25-hydroxyvitamin D3 24-hydroxylase enzyme activity in said control sample, at a given level of vitamin D receptor activity indicates the need for an adjuvant cancer therapy.

45. The method of claim 44, wherein said level 25-hydroxyvitamin D3 24-hydroxylase enzyme activity is measured in said biological sample and said control sample at the same vitamin D receptor activity or the activity levels are normalized to the level of vitamin D receptor activity in the sample and control.

46. The method of claim 33, wherein said animal is a mammal selected from the group consisting of humans, non-human primates, canines, felines, murines, bovines, equines, porcines, and lagomorphs.

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47. The method of claim 33, wherein said biological sample is selected from the group consisting of excised tissue, whole blood, serum, plasma, cerebrospinal fluid, buccal scrape, saliva, and urine.

48. The method of claim 33, wherein the difference between said increased level of *CYP24* in said biological sample and the level of *CYP24* in said control sample is a statistically significant difference.

49. The method of claim 33, wherein said increased level of *CYP24* in said biological sample is at least about 2-fold greater than the level of *CYP24* in said control sample.

50. The method of claim 33, wherein said increased level of *CYP24* in said biological sample is at least about 4-fold greater than the level of *CYP24* in said control sample.

51. A method of screening a test agent for the ability to inhibit proliferation of a *CYP24*-expressing cell, said method comprising:
(i) contacting said *CYP24*-expressing cell with said test agent; and
(ii) detecting the level of *CYP24* activity;
wherein a decreased level of *CYP24* activity as compared to the level of *CYP24* activity in a cell not contacted with said agent indicates that said agent inhibits proliferation of said cell.

52. The method of claim 51, wherein said cell is contacted with vitamin D.

53. The method of claim 51, wherein said detecting comprises detecting the level of *CYP24* mRNA, wherein a decreased level of *CYP24* mRNA in said *CYP24*-expressing cell as compared to the *CYP24* mRNA level in a cell not contacted with said agent sample, at a given level of vitamin D receptor activity indicates that said agent inhibits proliferation of said cell.

54. The method of claim 51, wherein said detecting comprises hybridizing a nucleic acid from said cell to an array of nucleic acid probes.

55.   The method of claim 51, wherein said detecting comprises detecting the level of *CYP24* protein, wherein a decreased level of *CYP24* protein in said *CYP24*-expressing cell as compared to the *CYP24* protein level in a cell not contacted with said agent sample indicates that said agent inhibits proliferation of said cell.

56.   The method of claim 55, wherein said level of *CYP24* protein in said contacted cell and said cell not contacted with said agent is measured at the same vitamin D receptor activity or the *CYP24* protein levels are normalized to the level of vitamin D receptor activity in the sample and control.

57.   The method of claim 51, wherein said detecting comprises detecting the level of 25-hydroxyvitamin D3 24-hydroxylase enzyme activity in said cell, wherein an decreased level of 25-hydroxyvitamin D3 24-hydroxylase enzyme activity in said *CYP24*-expressing cell as compared to the 25-hydroxyvitamin D3 24-hydroxylase enzyme activity level in a cell not contacted with said agent sample, at a given level of vitamin D receptor activity indicates that said agent inhibits proliferation of said cell.

58.   The method of claim 57, wherein said level of 25-hydroxyvitamin D3 24-hydroxylase enzyme activity in said contacted cell and said cell not contacted with said agent is measured at the same vitamin D receptor activity or the activity protein levels are normalized to the level of vitamin D receptor activity in the sample and control.

59.   The method of claim 51, wherein said *CYP24*-expressing cell is a tumor cell.

60.   The method of claim 51, wherein said *CYP24*-expressing cell is a hyperproliferative cell.

61.   The method of claim 51, wherein the difference between said decreased level of *CYP24* activity and the level of *CYP24* activity in a cell not contacted with said agent is a statistically significant difference.

62.   The method of claim 51, wherein said decreased level of *CYP24* activity is at least about 2-fold lower than the level of *CYP24* activity in a cell not contacted with said agent.

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1   63.   The method of claim 51, wherein said decreased level of *CYP24*
2   activity is at least about 4-fold lower than the level of *CYP24* activity in a cell not contacted
3   with said agent.

1   64.   A method of decreasing the proliferation of a cell with an elevated
2   level of *CYP24*, said method comprising reducing the level of *CYP24* activity in said cell
3   using an inhibitor of *CYP24*.

1   65.   The method of claim 64, wherein said method further comprises
2   contacting the cell with vitamin D.

1   66.   The method of claim 64, wherein said cell is a tumor cell.

1   67.   The method of claim 66, wherein said tumor cell is selected from the
2   group consisting of breast cancer cells, prostate cancer cells, colorectal cancer cells,
3   leukemia cells, lymphomas, lung cancer cells, brain cancer cells, pancreatic cancer cells, and
4   ovarian cancer cells.

1   68.   The method of claim 64, wherein said cell is a hyperproliferative cell.

1   69.   The method of claim 64, wherein said cell is a metastatic cell.

1   70.   The method of claim 64, wherein said inhibitor is selected from the
2   group consisting of antisense oligonucleotides, ribozymes, repressors of *CYP24* gene
3   expression, competitive inhibitors of 25-hydroxyvitamin D3 24-hydroxylase activity, and
4   non-competitive inhibitors of 25-hydroxyvitamin D3 24-hydroxylase activity.